Microgravity Research in the Space Shuttle Era

Bradley Carpenter

Cells in Space
Neal Pellis

Physical Sciences in Microgravity
Bradley Carpenter
Iwan Alexander

Commerical Ventures Take Flight
Charles Walker

The Space Shuttle cargo capability in the early 1980s stimulated a wave of imaginative research. Space-based microgravity research gave new insights into technologies critical to the space program, medical research, and industry.

NASA dedicated over 20 shuttle missions to microgravity research as a primary payload, and many more missions carried microgravity research experiments as secondary payloads. The space agency's microgravity research strived to increase understanding of the effects of gravity on biological, chemical, and physical systems. Living systems benefited as well. Cells, as they adapted to microgravity, revealed new applications in biotechnology.

Shuttle-era microgravity research was international in scope, with contributions from European, Japanese, and Russian investigators as well as commercial ventures. Several missions in which the Spacelab module was the primary payload were either officially sponsored by a partner agency, such as the Japanese or German space agency, or they carried a large number of research experiments developed by, or shared with, international partners. NASA and its partners established close working relationships through their experience of working together on these missions. These collaborations have carried over to operation of the International Space Station (ISS) and will provide the foundation for international cooperation in future missions to explore space.

Much of the Space Shuttle's legacy continues in research currently under way on the ISS—research that is building a foundation of engineering knowledge now being applied in the design of vehicle systems for NASA's next generation of exploration missions.

Cells in Space

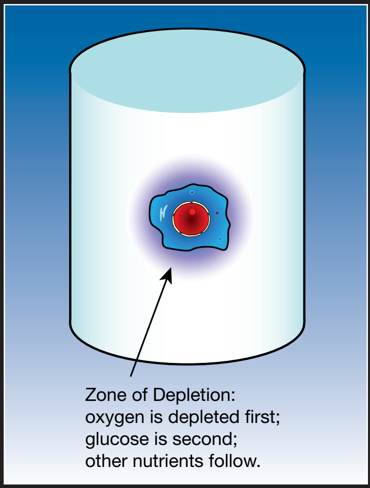
Question: ***Why fly cells in space?***

Answer: ***It helps in space exploration and provides novel approaches to human health research on Earth.***

The NASA Biotechnology Program sponsored human and animal cell research, and many of the agency's spacecraft laboratory modules supported the cell research and development necessary for space exploration and Earth applications. The shuttle, in particular, hosted experiments in cell biology, microbiology, and plant biology.

The rationale for studying cells in space is the same as it is on Earth. Cells can be a model for investigating various tissues, tumors, and diseases. NASA's work with cells can reveal characteristics of how terrestrial life adapts to the space environment as well as give rise to technologies and treatments that mitigate some of the problems humans experience in space exploration scenarios. Embarking on cell biology experiments in space spawned an almost revolutionary approach to accommodate cells in a controlled culture environment. The design of equipment for propagation of cells in microgravity involved special considerations that the Earth-based cell biologist seldom accommodates.

Cell Growth in Microgravity: Going Without the Flow



In the early stages of planning for cell culture in space, scientists theorized that cells may not survive for long because of a potential inability to assimilate nutrients from the culture fluid. Although undisturbed fluid appears not to be moving, gravity-driven convection mixes the fluid. Gravity continually moves colder, more dense fluid to the bottom of the vessel, displacing the warmer fluid to the top. As the fluid on the bottom is heated, the process is repeated. In space, there is no gravity-driven convection to mix the medium and keep nutrients well distributed and available to cells. Therefore, theoretically, cells should experience a decrease in the availability of nutrients, thus slowing assimilation down to their intrinsic rate of diffusion—a rate potentially insufficient to support life. Oxygen should be the first essential to be depleted within a matter of minutes, followed by glucose. In reality, the cells do not die. Instead, they adapt to the lower rate of nutrient delivery and proceed to survive. Apparently, other more subtle convections (e.g., surface tension driven) may supply sufficient transport of nutrients. Understanding these concepts was essential to the design of cell culture systems for humans in space.

Unique Conditions Created by Microgravity

In microgravity, gravity-driven convection is practically nonexistent. Gravity-driven convection is familiar to us in a different context. For example, air conditioners deliver cool air through the vents above. Cooler air is more dense than warm air and gravity settles the more dense cool air closer to the floor, thereby displacing the warm air up to be reprocessed. These same convective flows feed cells on Earth-based cultures where the cooler fluid streams toward the bottom of the vessel, displacing warmer medium to the upper regions of the container. This process provides sufficient nutrient transport for the cells to thrive.

What Happens in Microgravity?

Scientists theorized that, in microgravity, cells would rapidly assimilate nutrients from the medium and, in the absence of gravity-driven convection, the cells would consume all the nutrients around them. Nutrient transport and the mechanical sensing mechanism operate differently in the absence of gravity. NASA conducted research on the Space Shuttle over the last 2 decades of the program to elucidate the nature of cell response to microgravity and showed that, while most cell cultures can survive in microgravity, substantial adaptation is required. The outcome of this cellular research is the emergence of space cell biology as a new scientific discipline.

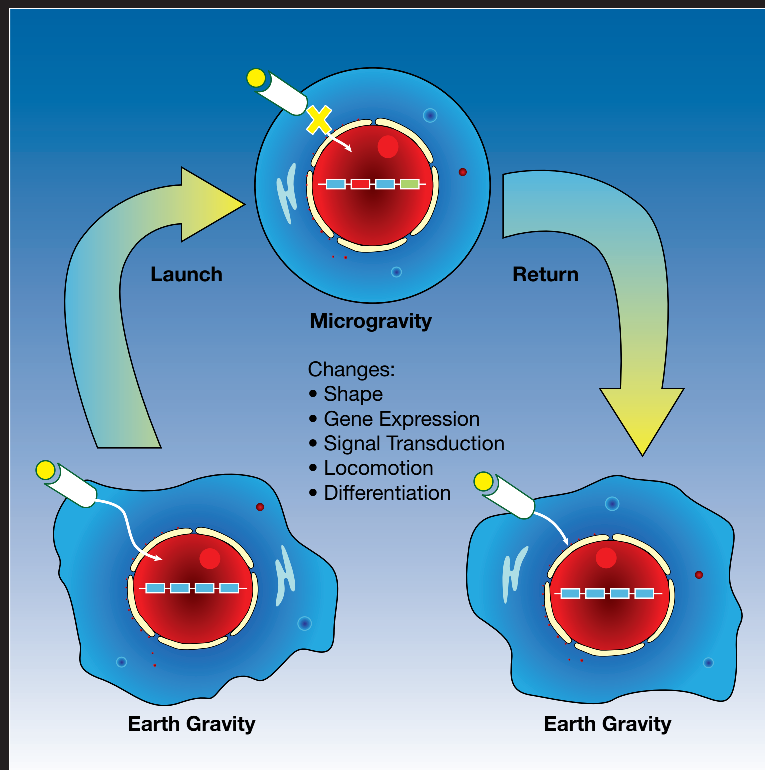
Suite of Equipment

To meet the various requirements for a full complement of cell biology experiments, NASA developed a suite of equipment that spans from relatively simple passive cell cultures to complicated space bioreactors with automated support systems. The experiments that were supported included space cellular and molecular biology, tissue engineering, disease modeling, and biotechnology. Space cell biology includes understanding the adaptive response to microgravity in the context of metabolism, morphology, and gene expression, and how cells relate to each other and to their environment.

Analog and Flight Research

The cell culture in space, and to a certain extent in microgravity analogs, is an environment where mammalian cells will associate with each other spontaneously, in contrast to Earth culture where cells sediment to the lower surface of the container and grows as a sheet that is one cell layer thick. In space and in an analog culture, the association results in the assembly of small tissue constructs. A construct may be made up of a single type of cell, or it may be designed to contain several types of cells. As the assembly proceeds, cells divide and undergo a process of differentiation where they specialize into functions characteristic of their tissue of origin. For example, as liver cells go through this process, they produce constructs that look and function akin to a native liver specimen. In other instances, colon cancer cells mixed with normal cells will produce assemblies that look and act like a fresh tumor biopsy.

Transition of Cells



As cells transition to space, changes occur that provide new insights into life systems and offer the prospect of understanding the role of gravity in life as it developed on this planet. A stylized cell with its nucleus (red) containing genetic material (blocks), an example of a cell surface receptor and its communication linkage to the nucleus, and the external simulating factor (yellow ball) are displayed above in three phases: 1) on Earth at unit gravity; 2) following launch into microgravity; and 3) return to Earth. Within a few seconds after arriving in microgravity, the cell becomes round and, thereafter, a cascade of changes follows over the next few days and weeks. As the cell adapts to the new environment, it turns on some genes and turns off others. The ability to respond to certain external stimuli is diminished. This is due to a disruption (indicated by the " ✖ ") of some cell surface receptor signal transduction pathways. In addition, cells locomote (move) very poorly in microgravity. The ability to mature and develop into functional tissues and systems seems to be favored. These observations provide a basis for robust investigation of microgravity cell biology as a means to understand terrestrial life in space and to use the space environment to foster goals in biomedical research on Earth.

These microgravity-inspired technologies are now used in cell culture and some tissue engineering studies. Scientists and physicians can produce tissues to be used as research models (e.g., cardiac tissues; cancers of the kidney, liver, colon, prostate, breast, and brain). Microgravity cultures are used in biotechnology to produce cell by-products that can be used to treat diseases and produce vaccines to prevent diseases.

NASA Develops Special Equipment to Grow Cells—Space Bioreactor

The use of microgravity cell culture to engineer tissues from individual cells began in systems where cells were grown in a tubular vessel containing a bundle of hollow fibers that carried nutrients to the cells in the tube. As concepts for space bioreactors matured, the cylindrical rotating systems emerged because of several advantages: greater volume; a format that supported both analog culture on Earth and space cell culture; and a natural association of cells with each other rather than with the plastic or glass vessel. The system could be rendered compatible with Earth or space by setting the rotation regime to the gravitational conditions. NASA performed a validation of the first rotating bioreactor system on Space Transportation System (STS)-44 (1991). No cells were used for the validation test. Instead, scientists used small beads made of inert polymer as surrogate cells. This enabled observation of the media delivery system and movement of "cells" along flow streams in the culture fluid. Results of the experiment showed characteristics consistent with maintaining live cells and set the stage for the first rotating bioreactor experiments in space.

Mary Ellen Weber, PhD
Astronaut on STS-70 (1995) and STS-101 (2000).

Colon Cancer Cells' unique response in microgravity: reassembly and reconstruction of their tissue origin.

Astronaut Mary Ellen Weber with the space bioreactor on STS-70.

"One of my fondest memories of my shuttle missions was working preflight with the bioreactor team on its first experiment in space. I can still vividly remember my awe in watching colon cancer cells growing into cancer tissue, and the satisfaction in seeing it all come together. The experiment held so much promise early on that it was manifested on the mission well before all its details were worked out, and this gave me, its assigned crew member, the opportunity to work far more closely with these dedicated scientists than usual in getting it ready to go as well as the opportunity to learn far more about the science. Most researchers get to see their hard work come to fruition first hand, and as I watched the bioreactor successfully working in space, I was really struck—unexpectedly so—by the fact that they could not be there to witness it with me. It gave me a great sense of responsibility to do right by them, and it made me all the more proud to be a part of it."

The first investigation on the shuttle (STS-70 [1995]) used colon cancer cells as the test population to determine whether the new bioreactor system was compatible with cell assembly, growth, and maturation. The bioreactor was composed of a cylindrical culture vessel, culture medium reservoir, waste reservoir, pump (functions as a heart), and gas exchange module that delivered oxygen and removed carbon dioxide (essentially acting as a lung). The results showed that microgravity afforded continuous suspension of the cells, spontaneous association, cell propagation, and formation of a tissue construct.

The space bioreactor facilitated rapid assembly, substantially larger constructs, and metabolically active cells. The experiment confirmed the hypothesis that microgravity facilitates tissue morphogenesis (formation) and set the stage for use of the space environment to identify the essential stages in tissue engineering that are novel to microgravity. The ability to engineer tissue from individual cells provided tissue for research, drug testing, disease modeling and, eventually, transplantation into afflicted individuals. Subsequent colon cancer experiments on STS-85 (1997) identified some of the novel metabolic properties and demonstrated the mechanism used by the cancer to spread to other organs.

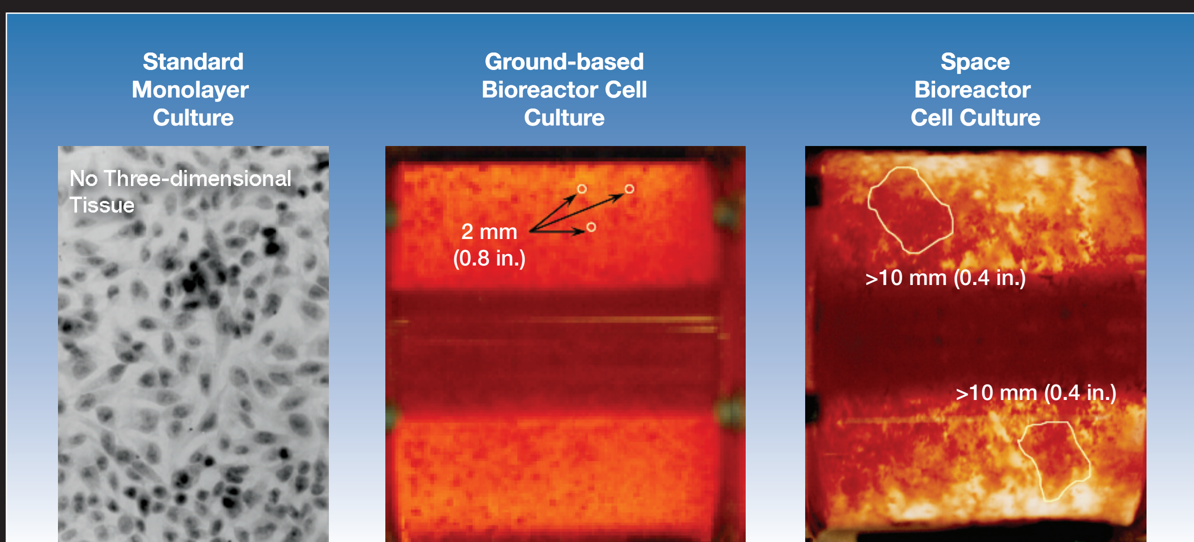
Interest in space cell culture opened the new vista of space cell biology. Mammalian cells are enclosed by a pliable lipid membrane. On Earth, those cells have a characteristic shape; however, when in microgravity, most mammalian cells become more spherical. Following this shape change, a cascade of adaptive changes occurs. Some genes are turned on while others are turned off, some receptors on the surfaces of cells cease to transduce signals to the inside, many cells cease locomotion (movement), and other cells will mature and change function spontaneously.

Microgravity-induced Changes at the Cell Level

Cells Adapt to Microgravity

On STS-62 (1994), NASA demonstrated that cells could grow in microgravity culture without succumbing to the lack of convective mixing of the medium. This demonstration occurred in a static culture system wherein rapidly dividing colon cancer cells and slowly dividing cartilage cells were placed in small culture vessels held at 4°C (39°F) (refrigeration temperature) until arriving in microgravity and reaching

Colon Cancer Cell Cultures



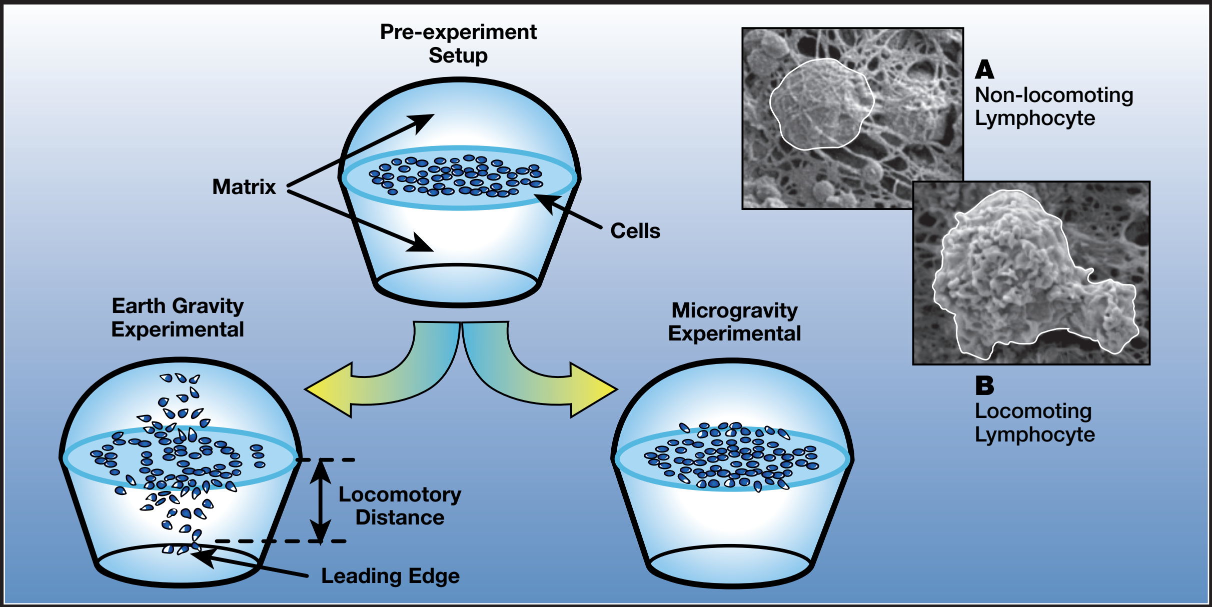
The first experiment using living tissue in the space bioreactor developed at Johnson Space Center used human colon cancer cells to determine whether there are specific advantages to propagation of cells in space. NASA conducted this experiment on STS-70 (1995) and again on STS-85 (1997). The right panel shows the large tissue assemblies that readily formed within a few days in microgravity when compared with the ground-based bioreactor analog, where the assemblies were much smaller and less well developed. For reference, the left panel shows the same cells in standard culture on Earth, where the cells grew and attached to the petri dish in a single layer with little evidence of tissue formation. This experiment set the stage for using space cell culture to produce tissues with a greater parity to the actual tumor in situ in the patient. Furthermore, unlike the standard culture, it demonstrated the signature biochemicals associated with the disease.

orbit where the temperature was raised to 37°C (98.6°F) (body temperature) to initiate growth. Results showed that colon cancer cells rapidly assimilated nutrients from the medium while cartilage took more than twice as long to deplete nutrients. Neither cell population succumbed to the depletion but, rather, changed their metabolic profile to adapt to more stringent conditions. Thus, bioreactors to support these cells for long-term experiments needed to accommodate re-feeding and waste disposal to ensure health of the tissue. The results of this experiment set the requirements for final design of the space bioreactors to grow bulk culture in microgravity.

Immune Cells Have Diminished Locomotion in Microgravity

The immune cells known as lymphocytes locomote and traverse many environments within the body to engage invading microbes and effect their destruction or inactivation. Experiments conducted on STS-54 (1993) and STS-56 (1993) were the first

Cell Locomotion



Human immune cells (lymphocytes) locomote through tissue matrix (intercellular cement) as part of their normal function in mediating immunity. Experiments performed in the analog culture system indicated a profound loss of the ability to locomote through matrix. This experiment described above was performed on STS-54 (1993) and STS-56 (1993). The matrix material is gelled collagen cast in two separate upper and lower phases, and the interface is loaded with human lymphocytes. Some were incubated as ground controls and others were transported to the shuttle. Locomotion remained arrested throughout the preparation and transport to space by maintaining them at 4°C (39°F). Upon arrival in microgravity, the temperature was raised to 37°C (99°F) in the experimental and control specimens. The lower left control shows how the lymphocytes locomote symmetrically up and down. Distance of locomotion to the leading edge can be measured using a microscope. In space, the experimental specimens evidenced very little locomotion. Non-locomoting lymphocytes are round and incapable of deforming (photo A), whereas locomoting lymphocytes deform and extend the process toward the direction of movement (photo B). The loss of locomotion in space indicates a potential defect in immunity in space. Loss of locomotion for extended periods of time can profoundly impact immunity. Locomotion is essential to this trafficking of lymphocytes through lymphoid organs and to sites of infection or invasion by cancer cells.

to show that these important immune cells have diminished locomotion in microgravity. Lymphocytes from a total of six donors were introduced into natural matrix (collagen) and kept at 4°C (39°F) until achieving orbit, where the temperature was raised to 37°C (98.6°F). Results showed that locomotion was inhibited by more than 80% in all specimens. Locomotion is a critical function in the immune system. Cessation does not have immediate effects; however, if sustained, it can contribute to a decline in immune function in space. Preparation for long-duration (in excess of 1 year) excursions in space will require extensive research and preparation to ensure the immune system functions normally throughout the entire mission. From strictly a cell biology perspective, the experiment was a milestone demonstration that locomotion can be modulated by a physical factor (gravity) rather than a biochemical factor.

Gene Expression Changes

Gene expression—defined as which genes are turn on and/or off in response to changing conditions—changes with almost every stimulus, stress, or alteration offered by our environment and activities. Most of these responses at the gene level occur in suites of genes that have been refined through evolution. This is why life systems can adapt to various environmental stimuli to survive and even thrive. Since all Earth organisms evolved in Earth gravity, the effect of microgravity on these genetic suites was unknown. Understanding the response at the genetic level to microgravity will give new insights to the changes necessary for adaptation.

New technology allows for the investigation of changes in more than 10,000 genes in a single experiment. The first genetic signatures for cells in microgravity were conducted on STS-106 (2000) using human kidney cells as a test model. The results provided a provocative revelation. Out of 10,000 genes tested, more than 1,600 were significantly changed in expression. Normally, a suite of genes refined through evolution is on the order of 20 to 40 genes. The enormous response to microgravity suggests there is not a refined suite, and the response is made up of genes that are essential to adaption—some are incidental and unrelated to adaptation, and some are consequential to the incidental activation of unnecessary genes. Analysis of gene expression showed that hypergravity (centrifugations at 3 gravitational force [*g*]) has a more refined set of about 70 genes. This is likely due to terrestrial life experiencing hypergravity during accelerations (running, starting, or stopping). On the other hand, analog microgravity culture on Earth also had a large response suite of 800 genes. Of those genes, only about 200 were shared with the microgravity suite.

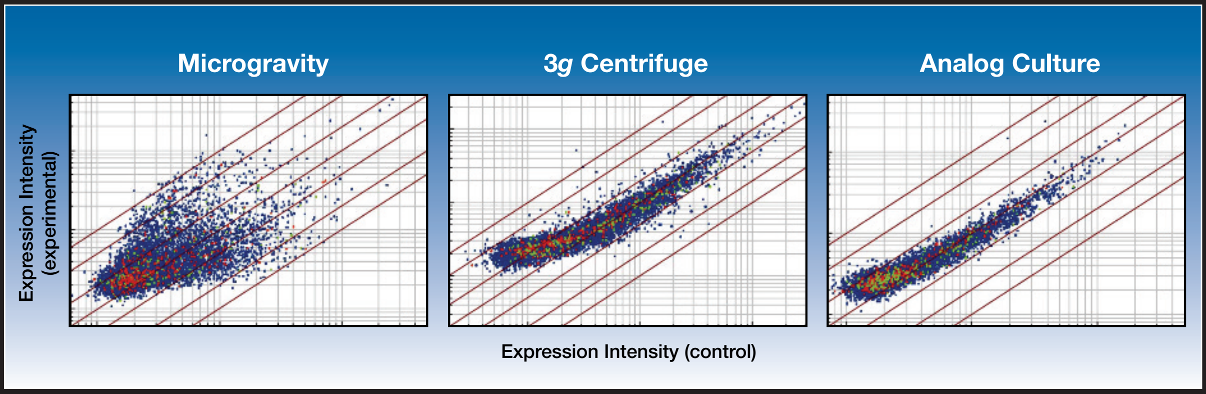
The significance of these results is multifold. For short-duration missions, we will want to manage any untoward effects brought about by the response. For long-duration missions in space and permanent habitation on planetary surfaces, we will want to know whether there is a refinement in the gene suite and whether, in conjunction with the new environment, it poses the possibility for permanent changes.

STS-105 (2001) hosted an experiment on human ovarian carcinoma, asking whether space cell culture gave a gene expression profile more like the actual tumor in the patient or like that observed in standard cell culture on Earth. Results showed tissue-like assemblies that expressed genes much in the same profile as in the tumor. This is significant because these results give scientists a more robust tool to identify specific targets for chemotherapy as well as other treatments.

Space cell culture offers a unique opportunity to observe life processes that otherwise may not be apparent. Forcing terrestrial life to muster its adaptive mechanisms to survive the new environment makes evident some new characteristic and capabilities of cells and other terrestrial life. One of the observations is the induction of differentiation (the process by which cells mature and specialize). The shuttle hosted numerous experiments that confirmed unique differentiation patterns in cancer cells from colon, ovary, and adrenals as well as human kidney cells and mouse cells that differentiate into red blood cells. All but the mouse cells were on STS-105. The mouse cell experiment was performed on STS-108 (2001).

In summary, these experiments opened a new understanding of the differentiation process and products of cells. The processes revealed aspects useful in proposing new approaches to treatment of disease and tissue engineering and to understanding complex developmental pathways. On the product side, materials were produced that may lead to new biopharmaceuticals, dietary supplements, and research tools.

Gene Expression Differs at Three Gravity Levels



NASA performed experiments using human kidney cell cultures on STS-105 (2001) and STS-106 (2000) to investigate the gene expression response to microgravity and compare it to hypergravity and to an analog culture system on Earth. In a sample set (10,000 genes), the genes turned on and off compared with the control in normal culture on Earth. If the expression is identical in control and experimental conditions, the dots line up on the diagonal line passing through the origin. Genes that are turned on are above and beyond the first parallel diagonal line. Genes below and beyond the first parallel diagonal are decreased in expression compared with the control. In microgravity, more than 1,600 of the 10,000 genes are up-regulated or down-regulated compared with the control, meaning that it is unlikely that terrestrial life has a preformed, inherited set of genes used to adapt to microgravity. The cells were then subjected to 3 gravitational force (*g*) using a centrifuge. The array is more compacted. Fewer than 70 genes are affected, suggesting that terrestrial life has a history of responding to hypergravity. The last panel shows the same cells in response to microgravity analog cell culture. More than 700 genes modified in response to the analog system that rotates the cell culture, such that the cells are falling continuously. Analysis indicated that it shared about 200 genes with that observed in microgravity.

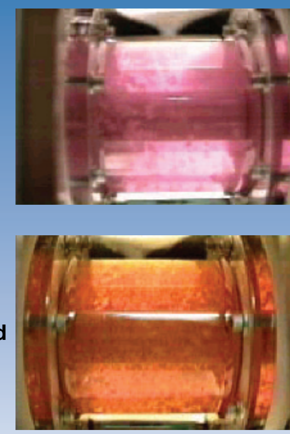
Observations from early experiments strongly suggested that the space environment may promote conditions that favor engineering of normal tissues for research and transplantation. Experiments in ground-based analog culture suggested that microgravity can facilitate engineering of functional cartilage starting from individual cells. (Cartilage is the tissue that forms the joints between bones.) Cartilage tissue was chosen because of its low metabolic demand on the culture system, durability, and conveniently observed characteristics of maturity and functionality. STS-79 (1996) flew a bioreactor containing beef cartilage cells to the Russian space station Mir. The culture set a landmark for 137 consecutive days of culture in microgravity. Results from this experiment and subsequent ground-based research: 1) confirmed the utility of microgravity in tissue engineering; 2) showed that generation of cartilage in microgravity produces a very pliable product when contrasted to native cartilage; and 3) showed that on transplantation the less mature, more pliable space cartilage remodels into the recipient site much better than mature cartilage. The study suggests that microgravity and space technology are useful in developing strategies for engineering tissues from a small number of cells.

Human Prostate Cancer Cells

On STS-107 (2003), NASA performed an experiment to investigate a model of metastatic prostate cancer. Prostate cancer is more manageable as a local disease, which is why there is such emphasis on preventive measures. Management of the disease becomes difficult when the tumor metastasizes to bone. Therein, the tumor establishes a relationship to that which contributes to its intractable state. Space cell culture offers an environment consistent with culturing two different kinds of cells harmoniously and also favors reassembly of cells into ordered tissue arrays. The upper cylinder shows the rapid assembly of the cells into tissue constructs that are much larger than those in the lower cylinder (controlled on Earth). The assemblies propagated in space achieved diameters approaching 2 cm (0.79 in.), while those on the ground were about 3 mm (0.19 in.). The result demonstrated the value of space cell culture in providing robust models for investigating human disease. These specimens were not analyzed, since they were not recovered from the ill-fated Columbia mission.

Flight

Ground



Coculture of Bone Marrow Stromal Cells and Prostate Cancer Cell Line

Human Prostate Cancer Cells Grew Well in Microgravity

In pursuit of using space to understand disease processes, NASA conducted experiments on STS-107 (2003) to understand the special relationship between prostate cancer and bone marrow cells. Prostate cancer, like breast cancer, is a glandular tumor that is a manageable disease when treated at its origin. In contrast, when tumors spread to other areas of the body, the disease becomes intractable. The experiment on STS-107 modeled the metastatic site in the bone for prostate cancer. Results showed the largest tissue constructs grown in space and demonstrated the outcome of the cohabitation of these two cell types. It also showed that we could produce these models for research and provide a platform for demonstrating the contribution of the normal cell environment to the establishment and maintenance of the tumor at a new site. With such a model, we may identify new targets for therapy that help prevent establishment of metastases.

The Future of Space Cell Biology

Research in cell science plays a significant role in space exploration. Cells, from bacteria to humans, are the basic unit of all life. As is true for Earth-based biomedical research in cells, the observations must be

Important Questions:

Does the cell respond directly to the change in gravitation force, or is it responding to conditions created by microgravity?

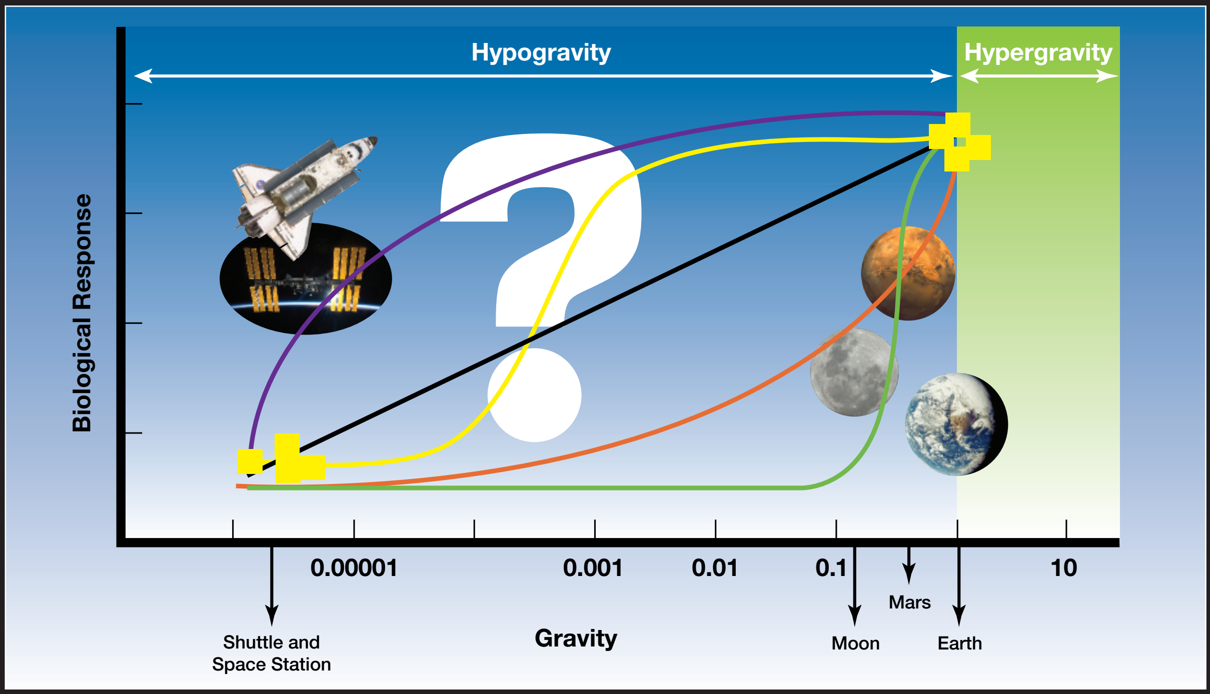
What does terrestrial life do to adapt and thrive in space?

Does microgravity influence how life might evolve after many generations in space?

What is the effect of microgravity on cells from major organs and the immune and digestive systems?

How much gravity is necessary to have normal function?

What Is the Relationship Between Gravity and Biological Responses?



The future of space cell biology includes a critical question regarding the relationship of gravity to various biological responses within the systems of the human body as well as in microbes, plants, animals, and bioprocessing systems. The possible relationships are depicted as lines on the graph, where values are known for the shuttle, space station, and Earth. The knowledge of the actual relationship will enable better understanding of human adaptability on the moon (1/6 gravitational force [*g*]) and Mars (3/8*g*). Furthermore, it will assist in the design of artificial *g* technologies. Knowledge of biologic responses on Earth reveals that the response relationships to stimuli are sigmoid, as in the yellow and green curve, and that the range of the response is usually within one tenfold increment of the normal physiologic state (Earth). Thus, the green relationship may be the most likely one. With this probability, research on moon and Mars gravity becomes more important in exploration planning. Depending where on the "*g*" scale the s-shaped part of the curve flexes, that is the amount of *g* that will begin to restore normal function.

consistent at the tissue, organ, and whole-organism level to be useful in developing treatments. Because we cannot perform experiments that may be difficult or even unethical in humans, biomedical researchers rely on cell-based research to investigate fundamental life process, diseases, and the effects of drugs and environment on life. Thus, part of our understanding of microgravity, hypogravity (such as the level found on Mars or the moon), radiation, and environmental factors will come from cell studies conducted in space and in analog culture systems.

The answer to the last question may have the most impact on risk reduction for humans exploring space. The answer will not only reveal the gravity force necessary to have acceptable physiologic function (bone health, muscle conditioning, gastrointestinal performance, etc.), it also may set requirements for the design of vehicles, habitats, exercise systems, and other countermeasures. The pervasive question is: How much gravity do you need? We do not know the mathematical basis of the relationship of gravity to biologic function. The history of research in space focused on microgravity (one millionth of Earth gravity) and, of course, there is a wealth of data on biologic function on Earth. Given these two sets of data, at least four different relationships can be envisioned. Of the four, the sigmoid (s-shaped) relationship is the most likely. The likely level for biological systems will be around 1/10*g*. Since the moon and Mars are 1/6 and 3/8*g*, respectively, it will be critically important that scientists have an opportunity to determine biological response levels and begin to conduct the mathematical relationship between *g* and biological function.

As NASA proceeds toward a phase of intensified use of the International Space Station (ISS) for research, it is important to have a robust plan that will continue the foundational research conducted on the shuttle and procure the answers that will reduce health risks to future spacefarers. When the United States enacted the national laboratory status of the ISS, it set the stage for all federal agencies to use the microgravity environment for their research. Increasing the science content of orbiting facilities will bring answers that will enable reduction of risks to explorers and help ensure mission success.

Physical Sciences in Microgravity

What is Gravity?

Gravity is a difficult thing to escape. It also turns out to be a difficult thing to explain. We all know enough to say that things fall because of gravity, but we don't have easy answers for how gravity works; i.e., how the mass of one object attracts the mass of another, or why the property that gives matter a gravitational attraction (gravitational mass) is apparently the same property that gives it momentum (inertial mass) when in motion. Gravity is a fundamental force in physics, but how gravity is bound to matter and how gravitational fields propagate in space and time are among the biggest questions in physics.

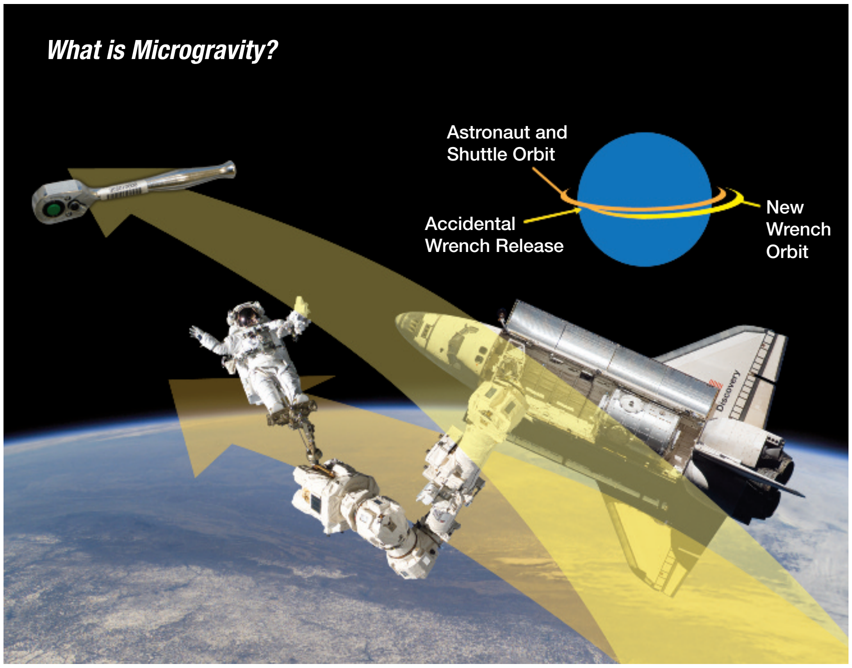
Regardless of how gravity works, it's clear that Earth's gravity field cannot be easily escaped—not even from a couple hundred miles from our planet's surface. If you stepped into a hypothetical space elevator and traveled to the 100,000th floor, you would weigh almost as much as you do on Earth's surface. That's because the force that the Earth exerts on your body decreases at a rate inversely proportional to twice your distance from the center of the Earth. In an orbit around the Earth, the force exerted by our planet's mass on a spacecraft and its contents keeps them continually falling toward the Earth with an acceleration inversely proportional to the square of the distance from the center of the planet. That's Newton's law of gravitation.

Gravity certainly works on and in airplanes. When you are traveling in an airplane during a steady flight, gravity keeps you firmly in your seat. The lift created by air flowing around the wings keeps an airplane and your seat aloft under you—and that's a good thing. Now imagine being in an airplane that has somehow turned off its lift. In this scenario, you would fall as fast as the airplane was falling. With your seat falling out from under you at the same rate, the seat would no longer feel your weight. No force would be holding you in it. In fact, you would be approximately weightless for a short period of time.

Weightlessness in Space

The essence of conquering gravity and sustaining weightlessness for longer than a few seconds is velocity. A spacecraft has to be moving very fast to continually fall toward Earth but still stay in space. Reaching that speed of a little over 27,500 km (17,000 miles) per hour provides a lot of the excitement of spaceflight. It takes a great deal of energy to put an object into Earth orbit, and that energy goes primarily into attaining orbital velocity. An astronaut in Earth orbit has kinetic energy equivalent to the explosion of around 454 kg (1,000 pounds) of TNT. Once an astronaut reaches orbital velocity, he or she is a long way toward the velocity needed to escape Earth's gravity, which is 1.4 times orbital velocity.

When you're in a vehicle moving fast enough to fall continually toward the Earth, it doesn't look or feel like you're falling. At least, not the kind of falling that people are accustomed to—the kind that ends in a painful collision with the ground. You have the feeling of being light, and the things around you are light, too. In fact, everything floats if not fastened to something. Items in the spacecraft are falling with



Imagine an astronaut tethered to the outside of the shuttle. The astronaut and the shuttle are in orbit together. If the astronaut releases a tool, the tool generally goes into a slightly different orbit because it has to maintain a different speed to achieve the same orbit as the shuttle. The astronaut, shuttle, and tool are in orbit with their outward acceleration from the Earth, balanced by Earth's gravity. The slight differences in orbit make it seem, to the astronaut, that a small acceleration is pushing the wrench away. This is microgravity.

you. With everything accelerating toward Earth at precisely the same rate within this falling frame of reference, Earth's gravity is not apparent. To an outside observer, gravity is still obvious—it's the reason you're in an orbit and not flying away from Earth in a line to space.

Early Low-gravity Technology

The consequences of being weightless were merely hypothetical until the dawn of space travel, with one small exception: One hundred years prior to the launch of the first rocket beyond Earth's atmosphere, spherical lead shot was manufactured by allowing molten lead to solidify in free fall inside a shot tower. As long as the shot wasn't falling fast enough for air resistance to deform it, the absence of gravitationally created hydrostatic pressure in the falling lead drop that allowed it to assume a spherical shape as the liquid was driven by thermodynamics into a volume of minimum exposed surface. The falling shot quickly hardened as it cooled, and it collected in a water bath at the bottom of the tower. The shot-manufacturing industry relied on this early low-gravity technology until the first decade of the 20th century.

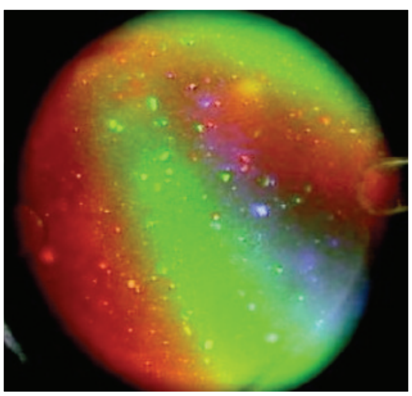
Physics Environment in Space

Spaceflight provides a good place to conduct experiments in physics—experiments that would not be possible on Earth. Wernher von Braun (center director at Marshall Space Flight Center from 1960 to 1970) had more practical applications, such as making ball bearings in space. Several simple experiments were flown on Apollo 14 and performed by the crew on the return from the moon. More experiments were conducted on the three Skylab missions—an early space station built in the 1970s—with promising results reported in areas such as semiconductor crystal growth. By the time of Skylab, however, the next era of space exploration was on the horizon with the approval of the Space Shuttle Program in 1972.

Fundamental Physics

One of the great questions of physics is the origin of long-range order in systems of many interacting particles. The concept of order among particles is a broad one—from simple measures of order, such as the density of a collection of molecules or the net magnetization of the atomic nuclei in an iron bar, to complex patterns formed by solidifying alloys, turbulent fluids, or even people milling about on an urban sidewalk. In each of these systems, the "particles" involved interact nearly exclusively with only their near neighbors; however, it's a common observation in nature that systems composed of many interacting elements display ordering or coherent structures over length scales much larger than the lengths describing the particles or the forces that act between them. The term for the distinctive large-scale behavior that results from cooperatively interacting constituent particles is "emergent phenomena." Emergent phenomena are of interest to science because they appear to be present at virtually every scale of the natural world—from the microscopic to the galactic—and they suggest that common principles underlie many different complex natural phenomena.

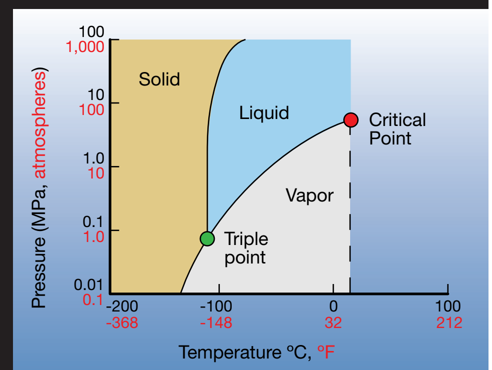
Phase transitions at a critical point provide physicists with a well-controlled model of an emergent phenomenon. Pure materials, as determined by thermodynamics, exist in a particular state (a "phase") that is a function only of temperature and pressure. At a point called a "critical point," simple single-phase behavior breaks down and collective fluctuations sweep through the system at all length scales—at least in theory. The leading theory that has been developed to describe emergent phenomena, such as critical point fluctuations, is called "renormalization group theory." It provides a model that explains how the behavior of a system near a critical point is similar over a large range of scales because the physical details of many interacting molecules appear to average out over those scales as a result of



Small particles in a colloidal solution assemble to form an ordered crystalline structure, such as the opalescent crystalline particles shown in this image taken on STS-73 (1995). Building an understanding of emergent phenomena remains one of the great challenges of physics. Explaining the origins of long-range order and structures in complex systems is key to advancing potential breakthroughs, and the experiments in fundamental physics aboard the shuttle played a significant role.

Critical Point Experiments Test Theories

The critical point of xenon is 289 K, 5.8 MPa—or 15.85°C (60.53°F), 57.2 atm. Note that the axis on the left is logarithmic. Research on STS-52 (1992) measured the phase boundary between normal liquid helium and superfluid helium. (Superfluids, such as supercooled helium-4, exhibit many unusual properties. The superfluid component has zero viscosity, zero entropy, and infinite thermal conductivity.) This shuttle research confirmed the renormalization group theory better than any Earth research. These types of research questions are now being studied on the International Space Station.



NASA tested the theory for gas-liquid critical phenomena on STS-97 (1997).

The Lambda Point Experiment cryostat assembly (identified by the JPL insignia) in the STS-52 (1992) payload bay.

cooperative behavior. Renormalization group theory is one of the great developments of physics during the 20th century. The most precise tests of this theory's predictions for critical point phenomena relied on experiments carried aboard the shuttle.

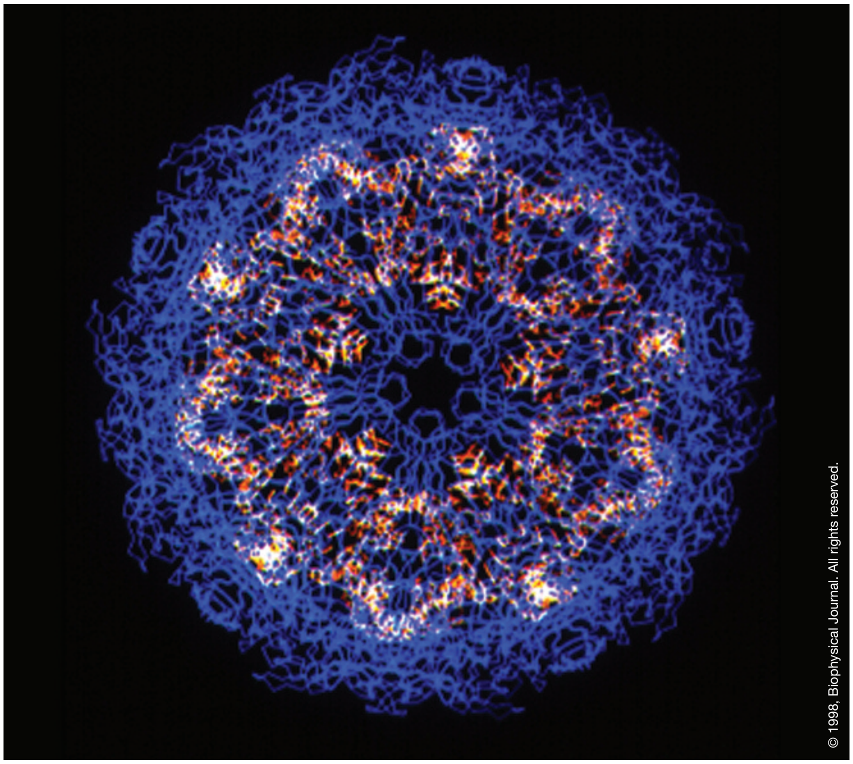
Careful critical point experiments required the ultimate in precise control of pressure and temperature to the extent that the difference in pressure, caused by gravity, between the top and the bottom of a small fluid sample in a laboratory on Earth by the mid 1970s became the limiting factor in experimental tests of renormalization group theory.

Research on Space Transportation System (STS)-52 (1992) measured the phase boundary between normal liquid helium and superfluid helium. Superfluids, such as supercooled helium-4, exhibit many unusual properties. The superfluid component has zero viscosity, zero entropy, and infinite thermal conductivity. This shuttle research confirmed the renormalization group theory better than any Earth research.

Protein Crystal Growth

A foundation for the explosion of knowledge in biological science over the past 50 years has been the understanding of the structure of molecules involved in biological functions. The most powerful tool for determining the structure of large biomolecules, such as proteins and DNA, is x-ray crystallography. In traditional x-ray crystallography, an x-ray beam is aimed at a crystal made of the molecule of interest. X-rays impacting the crystal are diffracted by the electron densities of each atom of each molecule arranged in a highly ordered crystal array. Because nearly each atom of each molecule is in a highly ordered and symmetrical crystal, the x-ray diffraction pattern with a good crystal is also highly ordered and contains information that can be used to determine the structure of the molecule. Obtaining high-quality protein crystals has been a critical step in determining a protein's three-dimensional structure since the time when Max Perutz first used x-ray crystallography to determine the structure of hemoglobin in 1959. A few proteins are easily crystallized. Most require laborious trial-and-error experimentation.

The first step in growing protein crystals is preparation of as pure a protein sample as can be obtained in quantity. This step was made easier for many molecules in recent years with the ability to increase the products of individual genes through gene amplification techniques; however, every purification step is still a tradeoff with loss of starting material and the likelihood that some of the molecules in solution will denature or permanently change their shape, effectively becoming contaminants to the native molecules. After biochemists have a reasonably pure sample in hand, they turn to crystal-growing recipes that vary many parameters and hunt for a combination that will produce suitable crystals. Although usable crystals can



This molecular structure of the Satellite Tobacco Mosaic Virus was captured at 1.8-angstrom (0.18-nanometer) resolution from analysis of crystals obtained on experiments performed on the International Microgravity Laboratory-2 mission (STS-65) in 1994. The best of these crystals was 30 times larger and produced 237% more data than any previous Earth-grown crystals and yielded what was, at that time, the highest-resolution structure of a virus ever obtained.

be as small as 0.1 mm (0.004 in.) on a side, the crystals often take weeks or even months to grow, so biochemists will normally try many combinations simultaneously and in specially designed trays. It is not unusual to spend several years finding good growth conditions for a protein.

Effects of Gravity on Protein Crystal Growth

Gravity has two principal effects in protein crystal growth. The first is to cause crystals to sink to the bottom of the solution in which they are growing. As a result, the growing crystals can pile up on each other and fuse, thus becoming a single mass that can't be used for data collection. The second effect of gravity is to produce weak but detectible liquid flow near the surface of the growing crystals. Having contributed some of its dissolved protein to the growing crystal, liquid near the crystal surface is lighter than liquid farther away. Due to gravity, the lighter liquid will rise. The consequences of this flow for crystal quality are complex and even now not fully understood. At the beginning of the shuttle era, German chemist Walter Littke thought that liquid flow near the growth surface would interfere with the molecules on the surface finding their places in a crystal. Before the first launch of the shuttle, he conducted several promising short rocket-launched experiments in which several minutes of low gravity were achieved in a suborbital flight.

Protein Crystallization on the Shuttle

The first protein crystallization experiments on the shuttle were conducted in a simple handheld device carried aboard in an astronaut's kit. Encouraging results from Professor Littke's experiment aboard STS-61A, the D-1 Spacelab mission (1985), where he reported achieving crystal volumes as much as 1,000 times larger than comparable Earth-based controls, opened a huge level of interest including many international and commercial investigators. Professor Charlie Bugg of the University of Alabama, Birmingham, working with Professor Larry DeLucas, who went on to fly on the US Microgravity Laboratory-1 mission (1992) as a payload specialist, eventually developed a community of nearly 100 investigators interested in flying proteins.

Some investigators obtained crystals that gave spectacular results, including the highest resolutions ever attained at the time for the structure of a virus and, in several instances, the first crystals suitable for structural analysis. Other proteins, however, seemed to show no benefit from space crystallization. A major focus of NASA's research was to explain this wide range of results.

Eugene Trinh, PhD
Payload Specialist and NASA expert in microgravity sciences on STS-50 (1992) US Microgravity Laboratory-1 Spacelab mission.

"The Space Shuttle gave scientists, for the first time, an opportunity to use the space environment as an experimental tool to rigorously probe the details of physical processes influenced by gravity to gather better theoretical insight and more accurate experimental data. This precious new information could not have been otherwise obtained. It furthered our fundamental understanding of nature and refined our practical earthbound industrial processes."


Eugene Trinh, PhD, a payload specialist for this mission, is working at the Drop Physics Module using the glove box inside the first US Microgravity Laboratory science module on STS-50.

Modeling Protein Crystal Growth

Physicists and biochemists constructed models of protein crystal growth processes to understand why some proteins produced better crystals in microgravity while others did not, and why crystals sometimes started growing well but later stopped. Investigators applied techniques like atomic force microscopy to examine the events involved in the formation of crystalline arrays by large and rather floppy protein molecules. The role of impurities in crystal growth and crystal quality was first documented through the work of Professor Alexander McPherson (University of California, Irvine), Professor Peter Vekilov (University of Houston, Texas), and Professor Robert Thorne (Cornell University, Ithaca, New York), along with many others. A simplified picture of a popular model is that proteins that grow better crystals in microgravity have small levels of contaminants in solution that preferentially adhere to the growing surface and slow the growth of the molecule-high step layers that form the crystal.

Accelerated transport of contaminant species due to buoyant flow on Earth will increase the population of contaminant species on the surface, eventually inducing the formation of defects. Such proteins will produce better crystals in microgravity because strongly adhering contaminants are transported by slower molecular diffusion rather than convection, and their surface concentration on the crystal remains lower.

This research has given a detailed scientific foundation to the art and technology of protein crystallization, thus providing structural biologists with a mechanistic understanding of one of their principal tools.

Biotechnology and Electrophoresis

In the 1970s and early 1980s, the biotechnology industry identified a large number of biological molecules with potential medical and research value. The industry discovered, however, that the difficulty of separating molecules of interest from the thousands of other molecules inside cells was a barrier to the production of therapeutic materials.

Separation techniques for biological molecules rely on using small differences between molecules to spatially separate the components of a mixture. The mobility differences that separation methods use can result from the size of the molecule, substrates to which the molecule binds, or charge on the molecule in solution.

Separation methods relying on the interaction of biological molecules with an applied electric field, including zone electrophoresis and isoelectric focusing, use the charge on a molecule that is dependent on the solution properties (pH, ionic strength, etc.) around the molecule to separate mixtures of molecules. The throughput and resolution of these techniques are limited by the flow induced in the solution containing the molecules, heat generated by the electric current passing through the liquid, and sedimentation of the large molecules during the necessary long separations. It was recognized that electrophoresis, one of the earliest candidates for space experiments, would solve the problem of the disruptive heat-driven flows by minimizing the effect of gravity. Warmer, lighter liquid wouldn't rise in the electrophoresis cell, and device performance might be dramatically improved.

Professor Milan Bier (University of Arizona, Tucson)—a pioneer in biological separations whose discoveries did much to establish electrophoresis as a laboratory tool—conducted several important flight experiments with NASA. As Professor Bier's work on the Isoelectric Focusing Experiment proceeded and flew on several early shuttle missions, he came to understand the impact of gravitational effects on Earth-based electrophoresis. He developed designs for electrophoresis equipment that minimized the impact of gravity. Within a few years, these designs became the industry standard and a basic tool of the biotechnology industry. Commercial organizations became interested in the potential of space-based bioseparations. McDonnell Douglas Astronautics Company sponsored seven flights of a large electrophoresis device—the Continuous Flow Electrophoresis System. Several flights included a McDonnell Douglas Astronautics Company technical expert who traveled on board as a payload specialist.

Using this facility on the shuttle middeck, Robert Snyder of the Marshall Space Flight Center, along with his colleagues, discovered a new mode of fluid behavior—electrohydrodynamic instability—that would limit the performance of electrophoresis devices even after the distortion of gravity was eliminated. The discovery of this instability in space experiments and subsequent confirmation by mathematical analysis allowed electrophoresis practitioners on Earth to refine their formulations of electrophoresis liquids to minimize the consequences of electrohydrodynamic effects on their separations. This led to experiments, conducted in a French-built facility by French pharmaceutical company Roussel-Uclaf SA, Paris.

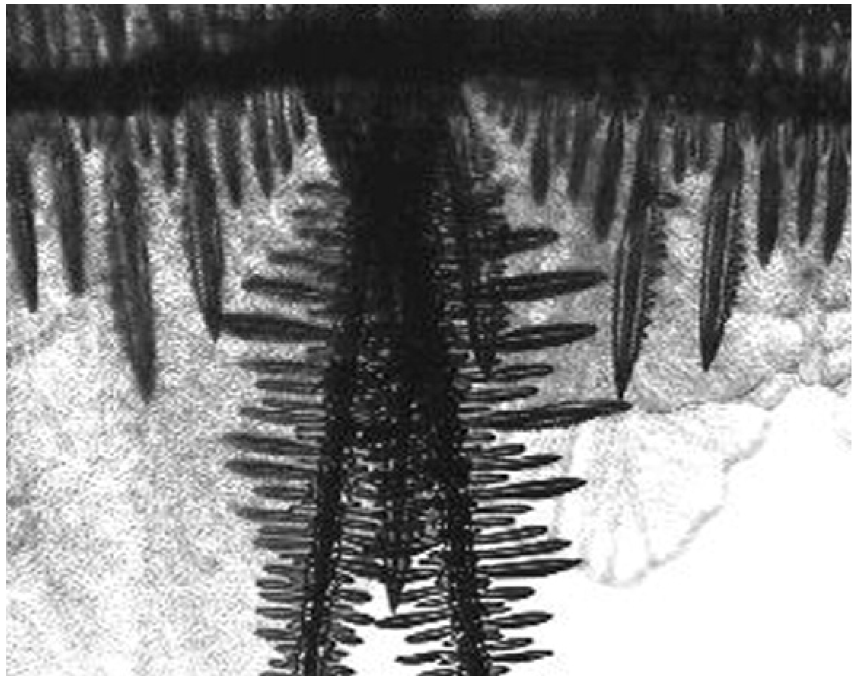
The opportunity to conduct sequential experiments of increasing complexity was one of the benefits of these shuttle microgravity missions. Interest shown by these commercial and international organizations initiated in early shuttle missions continues today on the International Space Station (ISS).

Materials Processing and Materials Science

The semiconductor industry grew up with the space program. The progression from commercial transistors appearing in the 1950s to the first integrated circuits in the 1960s and the first microprocessors in the 1970s was paralleled, enabled, and driven by the demanding requirements of space vehicles for lightweight, robust, efficient electronics.

Since the beginning of semiconductor technology, a critical issue has been the production of semiconductor crystals from which devices can be fabricated. As device technology advanced, more stringent device performance and manufacturing requirements on crystal size, homogeneity, and defect density demanded advances in crystal growth technology. In the production of semiconductor crystals, when molten semiconductor freezes to form a crystalline solid, variations in the temperature and composition of the liquid produce density variations that cause flows as less-dense fluid rises. These flows can cause poor distribution of the components of the molten material, leading to nonuniformities and crystal defects. Studying semiconductor crystal growth in low gravity, where buoyancy-driven flows would be extremely weak, would give insight into other factors at work in crystal growth. There was also hope that in microgravity, quiescent conditions could be attained in which crystallization would be "diffusion controlled" (i.e., controlled by stable, predictable mechanisms proportional to simple gradients of temperature and composition) and that, under these conditions, material of higher quality than was attainable on Earth would be produced.

In the early 1970s, semiconductor crystal growth was one of the first concepts identified by the National Research Council for materials processing in space. Promising early results, especially on Skylab, spurred plans for semiconductor research on the shuttle. Materials processing and semiconductor crystal growth experiments were also a prominent part of Soviet microgravity research. Crystal growth in space was a challenge because of the power needed by the furnaces and the containment required to meet NASA safety standards. Eventually, however, furnaces were built and flown on the shuttle not only by NASA but also by the European Space Agency and the space agencies of Japan, Germany, and France. Large furnaces flew on pallets in the cargo bay and in Spacelab while small furnaces flew on the shuttle middeck. To quantify the role of gravity in semiconductor crystal growth, NASA supported a comprehensive program of experiments and mathematical modeling to build an understanding of the physical processes involved in semiconductor crystal growth.



Solidification of a liquid is an unstable process under many conditions. An initially flat boundary will evolve into an elaborate web of branched dendrites. In metals, the properties of the resulting solid are highly dependent on the structure formed during solidification, making the understanding of interface evolution an important goal of materials science.

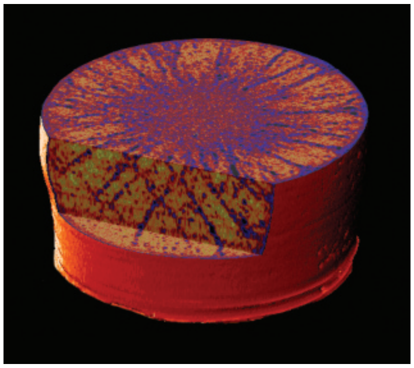
The results of materials processing and materials science experiments strongly influenced scientific understanding in several technologically important areas:

- Control of homogeneity and structural defects in semiconductor crystals
- Control of conditions for production of industrial alloys in processes like sintering and precipitation hardening
- Measurement of accurate thermophysical properties, such as surface tension, viscosities, and diffusivities, required for accurate process modeling

Liquid phase sintering experiments performed in low gravity yielded the unexpected results that the shape distortion of samples processed in microgravity is considerably greater than that of terrestrially processed samples. Sintering is a method for making objects from powder by heating the material in a sintering furnace below the material's melting point (solid state sintering) until its particles adhere to each other. Sintering is traditionally used to manufacture ceramic objects and has also found uses in fields such as powder metallurgy. This result led to improved understanding of the underlying causes of the shape changes of powder compacts during liquid-phase sintering with significant impact on a $1.8 billion/year industry.

Space experiments on the prediction and control of microstructure in solidifying alloys advanced theories of dendritic (from *dendron*, the Greek word for tree) growth and yielded important contributions to the understanding of the evolution of solid-liquid interface morphologies and the consequences for internal structure of the solid material. Introductions to metallurgy traditionally begin with a triangle made of three interconnected concepts: process, structure, and properties. According to this triangle, the study of metallurgy concerns how processing determines structure for various metals and alloys and also determines properties. A solidifying metal develops a characteristic structure on several distinct interacting length scales. The microstructure (usually on the scale of tens of microns) is formed by the typically dendritic pattern of growth of the solid interface. The macroscale pattern of a whole casting is determined by, among other things, the distribution of solutes rejected from the solid, shrinkage of the solid during freezing, and thermal conditions applied to the metal. The formation of structures during the solidification of practical systems is further complicated by the multiplicity of liquid and solid phases that are possible in alloys of multiple elements.

Understanding the processes that control the growth of dendrites on a growing solid is a foundation for how processing conditions determine the internal structure of a metal. Gravity can have a visible influence on the growth of dendrites because of the disruptive effects of flow caused by temperature gradients near the dendrite. Therefore, removing the effects of gravity was essential to obtain benchmark data on the growth rates, shapes, and branching behavior. In the 1990s, a series of experiments designed by Professor Martin Glicksman, then at the Rensselaer Polytechnic Institute, Troy, New York, was conducted on shuttle missions using an instrument named the Isothermal Dendritic Growth Experiment. The experiments carefully measured the characteristics of single growing dendrites in an optically transparent liquid; accurately determined the relationship among temperature, growth rate, and tip shape; and established the importance of long-range interactions between dendrites. Data from those experiments are widely used by scientists who work to improve the physical understanding and mathematical models of pattern formation in solidification.



These two samples show fracture patterns in sand at two different low confining pressures. The confining pressure is an equal, all-sided pressure that is experienced, for example, by rock at some depth in the Earth. Very low confining pressures are not obtainable on Earth due to gravity.

We learned the underlying physics of freckle formation (a defect in the formation alloy that changes its physical characteristics) from early results of materials research. It was shown that convection was directly responsible for the formation of freckles, and that rotating the sample can suppress freckle formation.

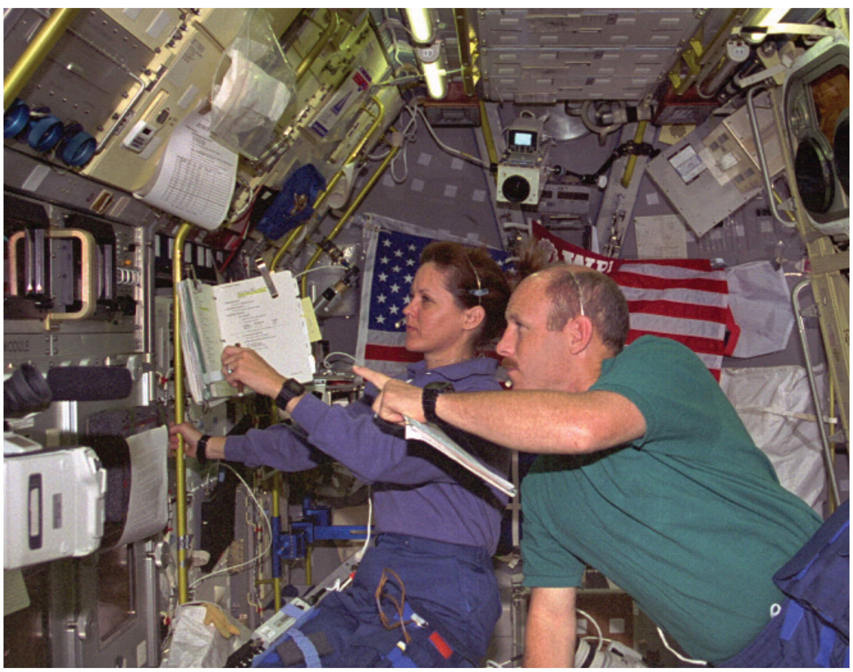
The contributions of the materials effort led to many innovations in crystal growth and solidification technology, including the use of magnetic fields, rotating crucibles, and temperature-control techniques. In addition, the analytical tools developed to understand the results of space experiments were a major contribution to the use of computational modeling as a tool for growth process control in manufacturing.

Fluid Behavior Changes in Space

Many people connect the concept of liquids in space with the familiar image of an astronaut playing with a wiggly sphere of orange juice. And, yes, liquids in space are fun and surprising. But, because many space systems that use liquids—from propulsion and thermal management to life support—involve aspects of spaceflight where surprises are not a very good idea, understanding the behavior of liquids in space became a well-established branch of fluid engineering.

The design of space vehicles—fluid and thermal management systems, in particular—made low gravity a practical concern for engineers. Decades before the space program began, airplane designers had to create fuel systems that would perform even if the plane were upside down or in free fall. Rocket and satellite designers, however, had to create systems that would operate without the friendly hand of gravity to put liquids at the bottom of a tank, let bubbles rise to the top of a liquid, and cool hot electronic equipment with the natural flow of rising hot air.

Without gravity, liquid fuel distributes itself in a way that minimizes its total free energy. For most fuels, liquid at the surface of the tank has a lower energy than the liquid itself, which means the fuel spreads out to wet the solid surfaces inside the tank. When bubbles are created in a fluid in space, in the absence of other factors the bubbles will sit where they are. Buoyancy, which causes bubbles to rise in liquids or hot air to rise around a flame, is the result of gravity producing a force proportional to density within a fluid. Many aspects of a vehicle design, such as its mechanical structure, are driven primarily by the large forces experienced during launch. For fluid and thermal systems, low gravity becomes a design driver.

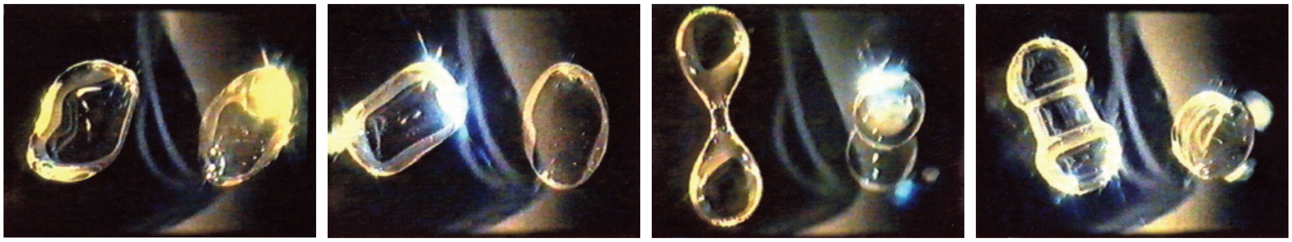


Astronauts Kathryn Thornton and Kenneth Bowersox observe a liquid drop's activity at the Drop Physics Module in the science module aboard the Earth-orbiting Space Shuttle Columbia (STS-73 [1995]). The two were joined by three other NASA astronauts and two guest researchers for almost 16 days of in-orbit research in support of the US Microgravity Laboratory mission.

A great deal of low gravity research performed in the 1960s focused on making liquid systems in space reliable. Low gravity experiments were performed by dropping the experiment from a tower or down a deep shaft or flying it in an aircraft on a parabolic trajectory that allowed the experiment to fall freely for about 20 seconds. The experiments possible in drop shafts and aircraft didn't allow enough time to test many technologies. As a result, engineers weren't sure how some familiar technologies would work in the space environment.

Low-gravity fluid engineering began with Apollo-era research focused on controlling liquid fuels; i.e., making sure liquid fuels didn't float around inside their tanks like an astronaut's orange juice. NASA performed most of this research in drop facilities, where experiments conducted in up to 5 seconds of free fall allowed basic ideas about fluid management to be investigated.

The arrival of the Space Shuttle opened the window for experiment duration from seconds to days and inspired the imaginations of scientists and engineers to explore new areas.

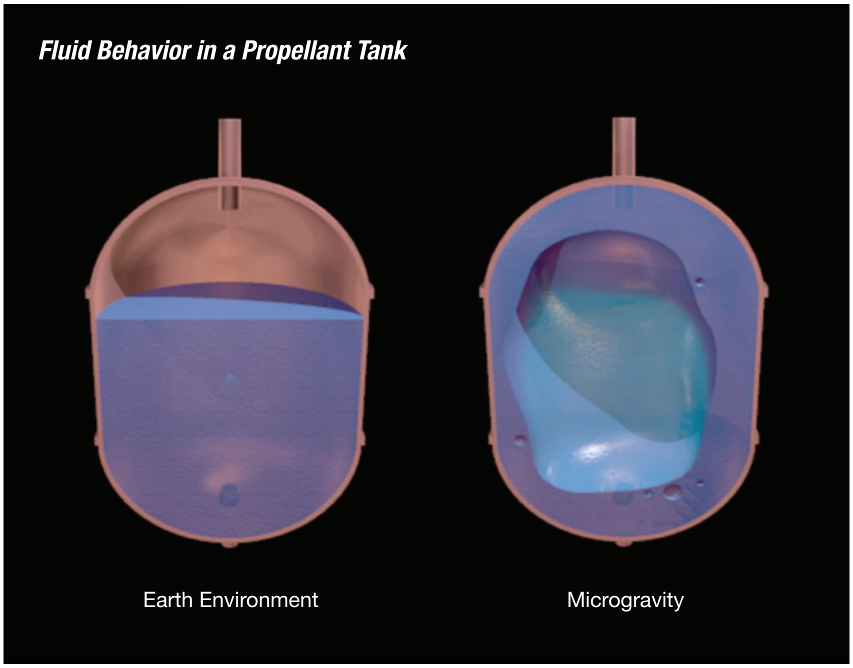


Drop physics experiments using advanced noncontact manipulating techniques on US Microgravity Laboratory (USML)-1 and USML-2 (STS-50 [1992] and STS-65 [1994], respectively) helped scientists understand the complex physical mechanisms underlying the seemingly simple processes of droplet shaping, splitting, and fusion.

The source of engineering problems with liquids in space is the partially filled container, or the gas-liquid interface. Without gravity, surface tension—the force that pulls a liquid drop into a sphere—together with the attraction of the liquid to the solid surfaces of the container determine the shape that a liquid will assume in a partially filled container.

To understand the unique behavior of liquids in space, researchers needed to look at the critical pieces of information in the liquid boundaries. Fluid physics experiments in the Spacelab Program, such as the Surface Tension-Driven Convection Experiment developed for Professor Simon Ostrach of Case Western Reserve University, Cleveland, Ohio, and the Drop Physics Module developed for Professors Robert Apfel of Yale University, New Haven, Connecticut, and Taylor Wang of Vanderbilt University, Nashville, Tennessee, led a wave of research into the properties of liquid interfaces and their roles in fluid motions. This research contributed to advances in other areas, such as microfluidics, in which the properties of liquid interfaces are important.

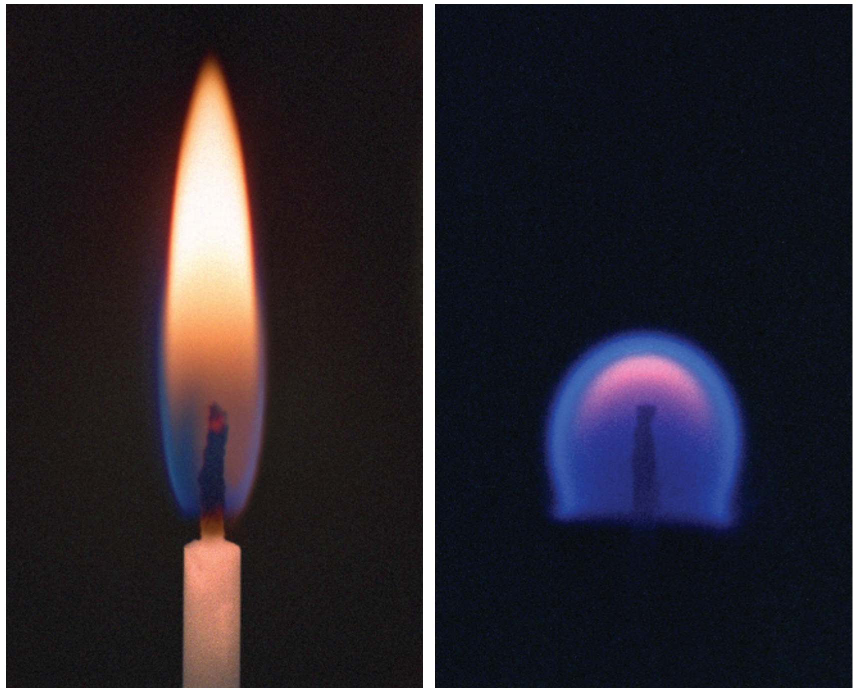
The shuttle enabled researchers to explore many new kinds of fluid behavior. Two examples out of many include: the Mechanics of Granular Materials experiment, and the Geophysical Fluid Flow Cell experiment. The Mechanics of Granular Materials experiment, developed by Professor Stein Sture at the University of Colorado, Boulder, examined the fluid-like behavior of loosely compressed soils and helped in understanding when and how, in situations like earthquakes, soils abruptly lose their load-bearing capability. Data from the experiment will also help engineers predict the performance of soils in future habitat foundations and roads on the moon, Mars, and other extraterrestrial



One of the earliest concerns about fluid behavior in microgravity was the management of propellants in spacecraft tanks as they orbited the Earth. On the ground, gravity pulls a fluid to a bottom of a tank (Earth environment, left). In orbit, fluid behavior depends on surface tension, viscosity, wetting effects with the container wall, and other factors. In some cases, a propellant can wet a tank and leave large gas bubbles in the center (microgravity, right). Similar problems can affect much smaller experiments using fluids in small spaces.

applications where the weight of the soil is much lower than on Earth.

The Geophysical Fluid Flow Cell experiment, developed by Professor John Hart at the University of Colorado, Boulder, used the microgravity environment to create a unique model of the internal motion in stars and gaseous planets, with a device that used an electric field to simulate gravity in a spherical geometry. The Geophysical Fluid Flow Cell flew on Spacelab 3 (1985), and again on US Microgravity Laboratory-2 (1995). Results from the experiment, which first appeared on the cover of *Science* magazine in 1986, provided many basic insights into the characteristics of gas flows in stars and gaseous planets. Hart and his colleagues were able to reproduce many of the flow patterns observed in gaseous planets under controlled and quantified conditions inside the Geophysical Fluid Flow Cell, thus providing a basis for analysis and physical interpretation of some of the distinctive dynamic features stars and gaseous planets.



This demonstrates the difference between flames on Earth (left) and in microgravity (right). The flame in microgravity is different because there is no upward buoyant force causing air to rise, so flames in space produce no buoyant convective flow that carry them upward.

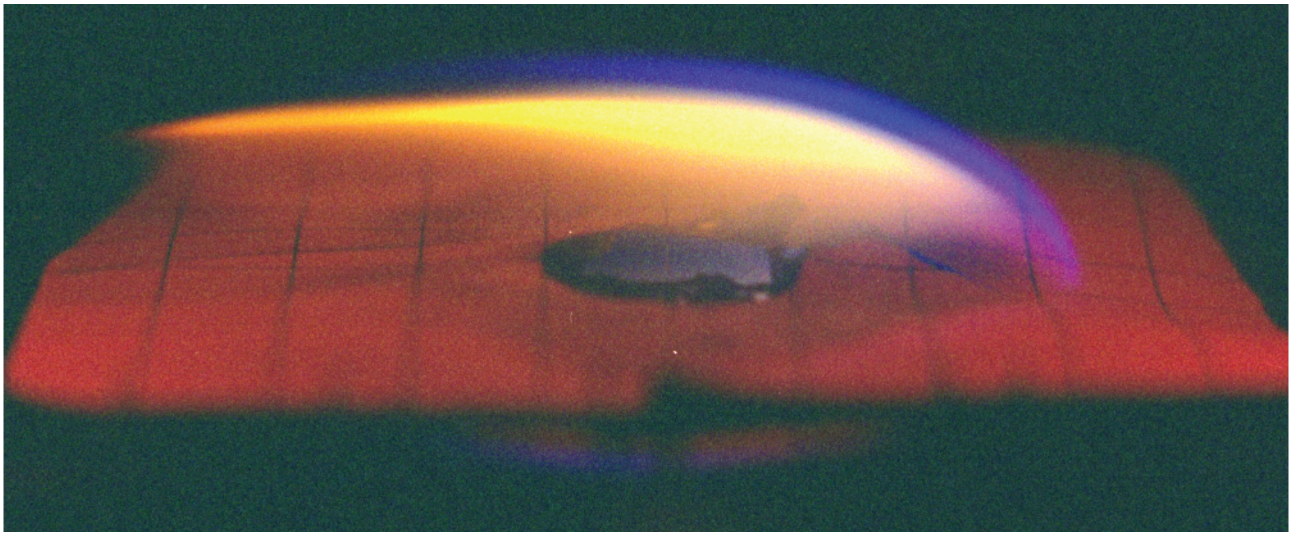
Combustion in Microgravity

What Is Fire Like in Microgravity?

The crew of a spacecraft has few options in the event of a major fire. Fortunately, fires in spacecraft are rare; however, because both rescue and escape are uncertain possibilities at best, fire prevention, detection, and suppression continue to be an ongoing focus of NASA research even after more than 30 years of study.

In the near-absence of gravity, fires ignite and spread differently than they do on Earth. Fires produce different combustion products, so experiments in space are essential to creating a science-based fire safety program. Research aboard the shuttle gave scientists an understanding of ignition, propagation, and suppression of fires in space. NASA is using the pioneering results of shuttle-era research to design a new generation of experiments for the ISS to help engineers design safer vehicles and better fire-suppression systems in the future.

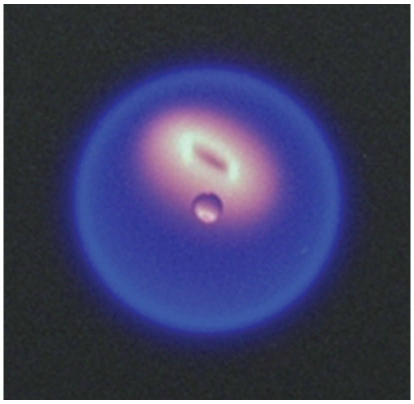
The biggest difference between space- and Earth-based fires is that on Earth, the heat released by combustion will cause a vigorous motion of the neighboring atmosphere as warm gas, less dense than the gas around it, rises due to its buoyancy under gravity. The upward buoyant flow draws surrounding air into the fire, increasing reaction rates and usually increasing the intensity of the fire. In space, buoyancy is negligible. Fire safety specialists must take into account the effects of cooling and ventilating airflows, which can significantly accelerate fires. Under “typical” conditions, however, combustion in space is slower than on Earth and is less complete. Soot particles are larger in space because particles spend more time growing in the fuel-rich reaction zone. As a result,



NASA fire safety experiments examined the effects of weak cabin airflows on fires. Here, a piece of paper burns in a flow like those used to cool avionics systems in space. NASA research showed that weak flows can have a strong influence on material flammability.

fire detectors in space need to be more sensitive to larger smoke particles than do fire detectors on Earth.

The experiments of David Urban of the NASA Glenn Research Center and his colleagues, included on the US Microgravity Payload-3 mission (1996), examined particulate-forming combustion in microgravity and observed that the larger particulates produced in microgravity were often not detected by the sensor technology employed in detectors deployed on the shuttle, even though the detectors worked reliably on Earth. An alternate technology more sensitive to large particulates provided superior detection. This technology, which uses scattering of a laser beam by particles in the airstream, is now deployed aboard the ISS.



In nearly perfect weightlessness, an ethanol droplet on the Microgravity Science Laboratory-1 mission in 1997 burns with a spherical flame.

Combustion of Fuels for Power

Beyond its initial motivation, combustion research on the shuttle also helped scientists better understand the basic processes of burning hydrocarbon fuels that according to the US Department of Energy provide the US economy with 85% of its energy. Research by Forman Williams of the University of California, San Diego, and Fred Dryer of Princeton University, New Jersey, and their students on the burning of fuel drops has been used by both General Electric (Fairfield, Connecticut) and Pratt & Whitney (East Hartford, Connecticut) to improve the jet engines they manufacture. Droplet combustion experiments in space produced well-controlled data that allowed Williams and Dryer to validate a comprehensive model for liquid fuel combustion. This model was integrated into the simulations that engine manufacturers use to optimize designs. Another experiment, led by Paul Ronney of the University of Southern California, Los Angeles, used microgravity to study the weakest flames ever created—100 times weaker than a birthday candle. Data on how combustion reactions behave near the limits of flammability were used to help design efficient hydrogen-burning engines that may eventually meet the need for clean transportation technologies.

Commercial Ventures Take Flight

Industry Access to Space Shuttle-inspired Innovation

NASA's charter included "seek and encourage … the fullest commercial use of space." Acting in that direction, NASA promoted the Space Shuttle during the 1970s as a platform for industry.

Private industry is in business to provide goods and services for a financial return. Innovation is important. Microgravity—a physical environment that was new to industry at the time—proved to be intriguing. High-efficiency processing and free-floating containerless manipulation and shaping of materials could become reality with an absence of convection, buoyancy, sedimentation, and density differentiation. Highly purified biological separations, new combinations and structures of materials with valuable properties, and contamination-free solidifications prepared in orbit and returned to Earth became industry objectives for prospective space processing research.

In 1985, NASA and the National Bureau of Standards were responsible for the first sale of a product created in space. Designated "Standard Research Material 1960," this product was highly uniform polystyrene latex microspheres (specifically, sizes of 10 and 30 micrometers mean diameter) used in the calibration of scientific and medical instruments. Dozens of companies purchased "space beads" for $350 per batch. This milestone came from an in-space investigation that produced both immediate science and an application.

Charles Walker
Payload specialist on STS-41D (1984), STS-51D (1985), and STS-61B (1985).

Charles Walker, payload specialist, works at the commercial Continuous Flow Electrophoresis System on STS-61B.

"As a corporate research engineer I had dreamed of building an industry in space. Business conducted in orbit for earthly benefit would be important. The Space Shuttle could begin that revolution.

"The first industry-government joint endeavor agreement, negotiated in 1979 between NASA and the McDonnell Douglas Astronautics Company, my employer, would facilitate space-enabled product research and development among different industrial sectors. It also presented an opportunity for me to realize that personal dream.

"NASA's astronauts had already successfully conducted limited company proprietary and public NASA research protocols during four flights with McDonnell Douglas' electrophoresis bioseparation equipment. Then NASA allowed one of our researchers to continue the work in person—exceedingly rare among researchers, and the first for industry.

"As the company's noncareer, non-NASA astronaut candidate, I had to pass the same medical and psychological screening as NASA's own. Training mixed in with my continuing laboratory work meant a frenzied year. Preparations for flight were exhilarating but they weren't free. McDonnell Douglas paid NASA for my flights as a payload specialist astronaut.

"Working with NASA and its contractor personnel was extraordinarily rewarding. I conducted successively more advanced applied commercial research and development as a crew member on board three shuttle missions over a 16-month period. It seemed the revolution had begun.

"I'm sorry to see these first-hand opportunities for applied research recede into history. Spaceflight is a unique, almost magical, laboratory environment. Disciplined research in microgravity can change human science and industry as surely as humanity's ancient experiences in the control of heat, pressure, and material composition."

For-profit businesses vary in their need for scientific research. Companies often prioritize the application (product) as more important than its scientific basis. For them, reliable, practical, and cost-effective process knowledge is sufficient to create marketable products. But, if convinced that research can add value, companies will seek it. Various industries looked at the shuttle as an applied science and technology laboratory and, perhaps, even a platform for space-based product production. Industry found that production was not especially feasible in small spacecraft such as the shuttle, but they were successful with scientific-technology advancements.

McDonnell Douglas' space-based research and development section was the first to fly on seven missions, and these missions took place from 1982 to 1985. The electrophoresis applications work was technically a success. It improved bio-separations over Earth gravitational force processing. For example, when a cell-cultured human hormone erythropoietin (an anemia therapy) was to be purified 100 times better than ground-based separations, a 223 times improvement was obtained. Protein product throughput per unit of time also improved 700 times. After the Challenger accident (Space Transportation System [STS]-51L) in 1986, access to space for commercial efforts was severely restricted, thus ending the business venture. The demonstration of possibilities, together with McDonnell Douglas' investments in ground-based cell culturing and assaying, made for the effort's enduring advances.

In 2009, Astrogenetix (Austin, Texas)—a subsidiary of Spacehab/Astrotech (Austin, Texas)—was organized to commercialize biotechnology products processed in microgravity. The company developed a proprietary means of assaying disease-related biomarkers through microgravity processing. This research objective was aimed at shortening and guiding drug development on Earth. From five rapid, shuttle-based flight opportunities (over a 15-month period), the company discovered a candidate for a salmonella vaccine. Even as Astrogenetix prepared to file an investigational new drug application with the US Food and Drug Administration, it was researching candidates for a methicillin-resistant Staphylococcus aureus vaccine. The company conducted this later work in microgravity on board the shuttle's final flights. Looking to the future, Astrogenetix is among the first commercial firms with an agreement from NASA for use of the International Space Station (ISS) national laboratory.

In the materials area, Paragon Vision Sciences (Mesa, Arizona) developed new contact lens polymers. During three flight experiments, the company looked into the effects of gravity-driven convection on long molecular chain formation, resulting in an improved ground-based process and Paragon's proprietary HDS® Technology materials product line.

Shuttle-based investigations amount to fewer than 6 months of laboratory time. Yet there have been significant outcomes across multiple disciplines. The national laboratory capability at the ISS seemingly offers a tremendous future of returns.